# COMMENTS TO "THE ETIOLOGY OF PORAL CLOSURE, AN EXPERIMENTAL STUDY OF MILIARIA RUBRA, BULLOUS IMPETIGO AND RELATED DISEASES OF THE SKIN. BY JOHN P. O'BRIEN, M.D."

MARION B. SULZBERGER, M.D., AND FRANZ HERRMANN, M.D.

*Post Graduate Medical School and Skin and Cancer Unit of New York University-Bellevue Medical Center.*

In the letter of January 12, 1950, which Dr. O'Brien sent together with the manuscript of his superb and masterly presentation, Dr. O'Brien has very kindly written to one of us as follows ". . . in view of your very special knowledge and interest in the subject, I would like to invite you to append a critical discussion at the end, as though we were both present at a meeting. There may be places too where you would like to add a footnote of commentary. These suggestions are prompted solely by a wish that truth and rapid progress should prevail." It is in this spirit that we accede to Dr. O'Brien's request and submit the following comments; we do this particularly because, as stated in Dr. O'Brien's letter, "all your own work as well as that of Shelley and Horvath (mentioned in the October '49 issue of the Journal of Investigative Dermatology) is not yet available."

John P. O'Brien is one of the most brilliant, fertile and indefatigable among the modern investigators of the local and systemic effects of poral closure and the sweat-retention syndrome. His present summary does him full justice, for it is indeed a beautiful presentation in regard to both the experimental findings and the careful and lucid form of demonstration. The microphotographs are unique examples of clarity and instructive value. Among the many illuminating histologic details, the keratin lining of the sweat pore aroused our special interest; the lining "dips down to surround a considerable length of the terminal portion of the sweat duct lumen" (compare Plate 2). This finding is in full accord with our own observations (obtained together with Keller and Pisha (4)) by vital staining with dyes used for examination in ordinary light, as well as with dyes employed for the study of fluorescence under filtered ultraviolet irradiation. These examinations have shown that in its electrical charges, and in many other respects, the structure along the lumen of the terminal portion of the sweat duct behaves like a keratin-coat.

Having been instructed by the author to voice frank criticisms, we admit that it is at present difficult for us to conceive poral closure or miliaria rubra as *primarily* due to the plugging effect of the bacterial agglomerations here demonstrated in the orifices. Our observations to date make us inclined to see the initial (primary) causes, as well as the essential and most common causes of the obstruction and poral closure as consisting of changes in the keratin, such as excessive formation and adherence, and particularly excessive hydration of the horny structures around and over the end part of the duct. The author himself offers similar considerations; and, among the early investigators, Pollitzer advocated this explanation of excessive hydration. We believe that some of the new

data here presented by O'Brien tend to support these older theories. In evaluating the effects of the salt-agar, it is necessary to bear in mind the extremely hydrophilic properties of the 8% sodium-chloride-containing agar which is, moreover, applied to the skin in a cup "under an ample amount of water-proof strapping." As shown by O'Brien in his control tests, "crystallina" appeared repeatedly under the agar cup even when the sites remained relatively sterile. We believe that the crux of the matter is that Dr. O'Brien is more inclined than we to set up a sharp line of separation between miliaria crystallina and miliaria rubra. Some of the more recent studies, which Dr. O'Brien was unfortunately unable to obtain and to evaluate before writing his summary, appear to support our idea that there seems to be a difference in degree, intensity and depth of closure rather than in the fundamental nature of the processes involved in miliaria crystallina and miliaria rubra (4, 7, 8). However, it is plausible to conceive that once there is closure, the bacterial and fungal and viral effects could well account for an intensification of the inflammatory reaction; and thus microorganisms would assume an important if "secondary" significance. When some skins are repeatedly and chronically exposed to high temperatures and humidities there is apparently set up a cycle of interdependent events which can lead to different forms of poral lesions, as well as follicular ones in some instances (e.g. tropical acne (5)). In brief, we feel that Dr. O'Brien may be inclined to emphasize somewhat too strongly the primary, stellar and solo role of infection in miliaria rubra in his statement: "Where infection is absent, edema and increased temperature are together capable of producing only a trivial and transient degree of poral closure, as manifested in crystallina." (Summary of Part II).

We agree wholeheartedly with the remarks of the author in the "Final Discussion of Poral Closure" that "the causes of closure of sweat pores are manifold", . . . and that "the actual chain of causation . . . probably varies from case to case and from one clinical entity to another."

It is due to the relatively recent efforts of different investigators that a number of quite different mechanisms have come to light, all of which may result in faulty and reduced outpouring of sweat. One of these mechanisms is horny plugging of the ostia of the ducts (2, 3); a second is blocking and poral occlusion through various other changes of the keratin (6, 7, 8); a third mechanism is the degenerative effacement of the straight portion of the ducts due to superficial atrophy and scarring (3); a fourth factor is the depletion of the surface waxes (9); and a fifth is probably the diminution of the electrophysiologic potential along the ducts (4); etc. It appears likely that still other mechanisms or components of the cycle leading to sweat retention will be revealed as time goes on. Any one of the possible factors demonstrated may be the predominant, perhaps the only, responsible influence in one instance; whereas a combined effect of several of these factors may occur or be essential in another. At present, we feel that the combined action of a number of factors occurs most commonly. It is then fully justified to regard each of the individual insults as a "*contributory*" factor, and difficult or impossible to ascertain which is primary. In this sense, we are in full agreement with the concept of the potentially important role of

bacterial growth at, and in, the openings of the ducts, as demonstrated so impressively in the present paper.

In closing our comments, we would like to leave the problem of infection and make one remark concerning the significance of the waxes on the skin surface. This is another factor to which O'Brien has devoted special attention and on which he has contributed vastly to our knowledge. Our own observations incline us to the thesis that the major acceleration of the outpouring of sweat is normally attributable to certain *hydrophilic properties* of the waxy surface film itself rather than to its dilating action on keratin rings. If we understand him correctly, O'Brien is inclined to attribute the major portion of the increased outpouring of sweat to the dilating effect of the waxes upon the keratin rings around the pores.

It has been a very real privilege to be able to follow the brilliantly original contributions of O'Brien in this field. Our comments show that there are only the smallest of minor divergences between his opinions and results and our own. We are in complete accord on almost all fundamentals. Our collaborators and we welcome Dr. O'Brien's masterly contributions to the elucidation of the decisive role of poral closure and of sweat retention in many important skin changes and in many aberrations of heat adaptation, of mineral and water metabolism, of adrenal and other endocrinologic responses, and of renal, pulmonary and cardiovascular functions.

## REFERENCES

1. Sulzberger, Marion B. and Zimmerman, H. M.: Studies on prickly heat. II. Experimental and histologic findings. J. Invest. Dermat. **7:** 61, 1946.
2. Sulzberger, Marion B., Zimmerman, H. M. and Emerson, Kendall, Jr.: Tropical anidrotic asthenia (thermogenic anidrosis) and its relationship to prickly heat. J. Invest. Dermat. **7:** 153, 1946.
3. Sulzberger, Marion B., Herrmann, F., and Zak, F. G.: Studies of sweating. I. Preliminary report with particular emphasis on a sweat retention syndrome. J. Invest. Dermat. **9:** 221, 1947.
4. Sulzberger, Marion B., Herrmann, F., Keller, R. and Pisha, B. V.: Studies of sweating. III. Experimental factors influencing the function of sweat ducts. J. Invest. Dermat. **14:** 911, 1950.
5. Sulzberger, Marion B., Addenbrooke, E. F., Joyce, S., Greenberg, S. and Mack, A. G.: Tropical acne. U. S. Naval Med. Res. Unit No. 2, U. S. Navy and U. S. Army Med. Dept. Bulletins, 1946.
6. Shelley, W. B., Horvath, P. N., Weidman, F. D. and Pillsbury, D. M.: Experimental miliaria in man: I. Production of sweat retention anidrosis and vesicles by means of iontophoresis. J. Invest. Dermat. **11:** 275, 1949.
7. Shelley, W. B. and Horvath, P. N.: Experimental miliaria in man. II. Production of sweat retention anidrosis and miliaria crystallina by various kinds of injury. J. Invest. Dermat. **14:** 9, 1950.
8. Shelley, W. B. and Horvath, P. N.: Experimental miliaria in man. III. Production of miliaria rubra (prickly heat). J. Invest. Dermat. In Press. (Read before the 10th annual meeting of the Society for Investigative Dermatology, Atlantic City, N. J., June 12, 1949.)
9. O'Brien, J. P.: A study of miliaria rubra, tropical anhidrosis and anhidrotic asthenia. Brit. J. Dermat. **59:** 125, 1947.